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*The Evaluation and Treatment of Male Infertility

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As the perpetuation of the species is primarily dependent upon its reproductive ability it is no wonder that the problem of sterile wedlock is one which has concerned mankind from time immemorial. Many references to the recognition and treatment of infertility may be found even in the earliest writings of man, and from those early times until the present there has been an unending quest for the answer to this problem, the path of which has led through many strange fields ranging from the divine to the witches brew. This is evidenced by the vast number of heathen, mythological, and other fabulous deities and powers in which the faculty of being able to restore fertility has been invested by credulous mankind. In China to-day for example statues of the goddess of fertility, Kwan Yen are to be seen with their kneeling stones almost worn away by the knees of countless thousands of barren women who, by supplication to this deity, believed that the blessing of fecundity would be bestowed upon them. Likewise the folklore of virtually every nation on earth contains many and varied, and often weird rites and ceremonies to say nothing of extraordinary recipes and formulae, all of which are believed capable of exorcizing the evil spirit of sterility.

Whether on this account or because of prejudice or because of ignorance, the fact remains that the scientific investigation of the barren marriage has been curiously delayed until comparatively recent years. For centuries the entire onus of infertility has always been placed on the woman and it was not until less than a century ago that the husband's aptitude for inducing pregnancy was ever questioned, and furthermore it is only in the last 25 years that this bitter blow to masculine pride has been more or less accepted, and that the scientific investigation of the barren marriage has included the routine evaluation of the husband's potentialities in this respect as well as those of the wife.

Prejudices which delayed progress in this direction were initially shared by the lay public and the medical profession alike. Dr. Marion Sims, the pioneer of the rational study of sterility, encountered tremendous opposition and no little abuse from his colleagues in America, when in 1868 he advocated semen examination and the demonstration of spermatozoa as a criterion of fertility in men. He was the first to make a post-coital examination of the cervical mucous, and when he described this test, which still bears his name, he was severely criticised in the medical Press of his day, one journal in particular stating that "this dabbling in the vagina with speculum and syringe was incompatible with decency and self respect." Enlightened views unfortunately often take time for their acceptance, and it was not until early in this century that medical prejudice was overcome and the teachings of Sims began to be recognised and put into regular practice.

Although medical prejudices have been overcome the battle as far as the lay public is concerned has not as yet been won. The necessity for systematic examination of the husband in a case of infertile union is an acknowledged fact by the medical profession. This view unfortunately is by no means universally accepted by the suspect husbands and there are still many who resent any question as to their reproductive ability and who resent even more the suggestion of any examination likely to cast doubt upon their manhood.

There are no doubt many reasons for this male antagonism, but probably the most important is the firm belief by many men that the capacity to be a husband is synonymous with the capacity to be a father; in other words, the ability to have sexual intercourse is ample proof of their fertility. Another strong reason for reluctance to undergo examination is the fear that not only may the examination reveal infertility with its attendant blow to masculine pride, but also the fear that evidence of previous disease, indiscretions, or sexual aberrations may thus be brought to light.

There are many other more or less subtle prejudices which make some husbands hesitant to submit to an examination, but all in all these prejudices and antagonisms are slowly disappearing, and the suspect husband is now putting his fragile ego in his pocket with far greater frequency, and accepting his possible responsibility in this matter with better grace than ever before.

These prejudices are mentioned not only because of the part they have played in delaying

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scientific investigation of male infertility, but also because they do still exist and must be fully recognised and tactfully dealt with by the practitioner if new converts to the cause are to be made.

Although this paper is limited to the question of infertility in the male it must be stressed at the outset that the study of infertility is complete only when it includes both marital partners.

Incidence of Barren Marriage:

Before a marriage can be considered possibly infertile it is obvious that a certain period of time must elapse during which no pregnancy ensues in spite of the couple leading a normal uncontracepted married life. Strictly speaking this should include the entire reproductive life of the couple, as a first pregnancy may not occur until after many years of normal married life. For practical purposes, however, the arbitary time limit of two years is generally accepted.

On the basis of this two-year limit about 10 per cent. of all marriages are infertile and of these the male is the responsible partner in 40 per cent, to 50 per cent. of cases. It is also estimated that in approximately 20 per cent. of infertile marriages both partners are to a greater or lesser degree at fault, a finding which underlines the importance of investigating both the male and the female and not exonerating the one merely because a cause for the infertile union is found in the other.

Causative Factors in Male Infertility

Before considering the various causes of male infertility it is as well to review the main factors upon which reproductive ability depend, as these form a basis not only on which a satisfactory classification of the causative factors can be made. but also from which a system for their evaluation and treatment can be evolved.

The factors concerned are:

(1) The ability to have normal sexual intercourse, i.e., potency.
(2) The possession of a normal genital tract.
(3) The production of germ plasm capable of fertilizing the ovum.

These factors are obviously closely interdependent, but any one or more of them is liable to a particular group of anomalies and disorders which, depending on their nature and severity, may result in relative or absolute infertility.

A simple classification of the etiological factors of male infertility may therefore be made, also under three main headings, each representing a deviation from the normal requirements for fertility just mentioned.

(a) Inability to have normal sexual intercourse, i.e., impotence.
(b) The presence of certain anomalies or disorders of the genital tract.
(c) The production of defective germ plasm incapable of fertilizing the ovum, i.e., defective spermatogenesis.

Each of these causative factors must be considered separately and in more detail.

(*a*) *Impotence*:

The inability to consummate the sexual act is due to a failure of any one of the three requisites of potency:— erection, intromission and ejaculation.

Erection is dependent upon an intact and functioning parasympathetic system through the second, third and fourth sacral nerves and is considerably influenced in its initiation and maintenance by the higher centres and the psyche. Any abnormality affecting normal function of these, therefore, may have disastrous effects on the power of erection.

Failure of erection may be due to local or general causes. The local causes include congenital abnormalities, injury to or disease processes of the penis. The general causes include general systemic disease and debility, disease or injury to the central nervous system or local peripheral nerves, e.g., cauda equina lesions, and psychogenic factors, this last being by far the most common cause.

Failure of intromission may be due to complete or partial failure of erection. Penile anomalities and deformities may also preclude intromission, even though partial erection is achieved. A less common, but no less important cause of failure of intromission is ignorance of marital technique on the part of the male. Many truly amazing cases have been reported and will no doubt continue to occur in the future. Not infrequently this lack of knowledge is found in men of high intellectual attainments, and it is therefore unwise to assume that any man is necessarily well acquainted with the technique of sexual intercourse, and in all cases a careful history of the patient's marital habits must be obtained, as the solution to an infertile union may well lie there.

Ejaculation is a complex function involving both the sacral parasympathetic outflow (second to fourth nerves) and the sympathetic nervous system.

The local causes of ejaculatory failure include congenital abnormalities, e.g. the more advanced cases of hypospadias where the semen is deposited outside the vagina, and retrograde ejaculation into the bladder which occurs when the function of internal vesical sphincter is destroyed as for example in prostatic surgery. Post-inflammatory lesions, particularly urethral stricture may also impede normal ejaculation.

It has been shown that bilateral sympathectomy involving L 1 ganglia results in loss of ejaculatory power in a high proportion of cases. As with erection, ejaculation is under the control of the higher centres, and the general causes of its failures may be found not only in psychogenic but also organic disturbances of the central nervous system.

(*b*) *Anomalies and Disorders of the Genital Tract*

Under this heading is included the congenital anomalies and obstructive lesions in so far as they prevent the access of the spermatozoa to the urethra. Such lesions must of course be bilateral to cause infertility.

Congenital anomalies of the epididymis and vas are not uncommon and represent varying degrees of failure in the development of the Wolffian system. Thus absence of the epididymis or vas or both in part or whole may occur and developmental strictures not only of the vas but also of the epididymal duct are more prevalent than is generally realized. Separation of the epididymis from the testis and also of the vas from the epididymis may likewise be encountered amongst the developmental disorders of this region. The former is not confined to undescended testis as formerly thought and may be found in normally descended organs.

Post-inflammatory stricture of the duct of the epididymis is a fairly common sequel to both non-specific and gonococcal epididymitis, but may also be traumatic in origin.

Similar strictures may occur in the vas and likewise traumatic division both accidental and deliberate occurs.

Chronic infections of the vesicles and prostate were long considered factors in low fertility. Contemporary opinion, however, is that there is little if any connection between prostatic infection and male infertility. Obstruction to the ejaculatory ducts may occur as a result of chronic infection, but is of rare occurrence.

(*c*) *Defective Spermatogenesis*

The production of defective germ plasm incapable of fertilizing the ovum implies qualitative and quantitative deficiencies not only in the spermatozoa but in the semen as a whole.

The production of normal semen is dependent upon a correctly functioning endocrine system, testes capable of reacting to this system by producing normal spermatozoa as well as androgens and oestrogens, and finally upon an intact spermatic tract which not only ensures the normal maturation and onward passage of the spermatozoa, but also provides the secretory contributions to the semen from the seminal vesicles and the prostate.

The physiology of testicular activity is not completely known, but the following simplified concept however is one which enjoys wide acceptance to-day.

The anterior lobe of the pituitary which itself is probably controlled by the hypothalamus produces two gonadotrophic hormones which have a fundamental affect on the testes.

(1) The follicle stimulating hormone (F.S.H.) or Prolan A. This controls the differentiation and function of the seminiferous tubules by acting on both the spermatogenic and Sertoli cells.

(2) The interstitial cell-stimulating hormone (I.C.S.H.), also known as the luteinising hormone (L.H.) or Prolan B. This controls interstitial (Leydig) cell differentiation and function. The mature Leydig cells in turn produce androgens (testosterone) and also it is thought, oestrogens. The testicular androgens probably in combination with those produced by the reticular cells of the adrenal cortex are responsible for the appearance and maintenance of the secondary sexual characteristics. These androgens and oestrogens also have a controlling influence on the pituitary by inhibiting the output of both the gonadotrophic hormones.

The structural units for spermatogenesis are the seminiferous tubules, each of which is from one to three feet in length, and, as each testis possesses about 300 to 600 of these units, the total length of the tubules is in the region of half a mile! The spermatozoa develop from the germinal cells in the tubules which are in a continuous process of maturation and division. Five stages have been recognised in this process ranging from the spermatogonium through the

primary and secondary spermatocyte to the spermatid and finally the spermatozoon which is set free in the lumen of the tubule. These testicular spermatozoa are in some way immature and not capable of fertilization. There is considerable experimental evidence to show that the fertilizing ability of the sperm progressively increases the further it migrates from the testis, so presumably maturation occurs in the epididymal duct and during its onward passage in the seminal tract. The means by which the sperms pass along the seminal tract is not definitely known, but it is generally accepted the sperms are not sufficiently motile to leave the epididymis under their own power, and therefore peristaltic action is the most likely propulsive force.

Spermatogenesis is a delicately balanced function which is easily upset by many different conditions, and when disturbed the spermatogenic deficiencies are reflected in the spermatozoa themselves. and may result in a decrease in numbers (oligozoospermia); or even their complete absence (azoospermia). Alterations of form and motility may also occur in varying degrees depending on the nature and severity of the upset. The significance of these deficiencies will be discussed later, and in the meantime the causes of spermatogenic failure will be considered.

The known conditions which may affect spermatogenesis are:

1. Congenital anomalies of the testis.
2. Acquired injury to the testes.
3. Endocrine disturbances.

There is a further large group of cases in which spermatogenic deficiency is present without demonstrable cause.

(1) *Congenital Anomalies of the Testis*

Under this heading is included not only the so-called congenital testicular aplasias but also undescended and ectopic testes, although it is difficult to be sure that these are not in fact primarily endocrine in origin.

It has long been known that cryptorchidism results in atrophy of the testes and damage to spermatogenesis. In the early years of the nineteenth century, Sir Astley Cooper taught that patients with bilateral retained testes were usually sterile, and the story goes that having told this to a class, one of his pupils, a cryptorchid, left the room and committed suicide. At the ensuing post mortem examination motile spermatozoa were demonstrated. The moral being that it is not wise to summarily pronounce a cryptorchid as being incapable of parentage. If only one testis is undescended there is not much danger of impairment of fertility provided that the descended organ is normal.

As far back as 1892 Griffiths found the testes of a dog underwent degenerative changes if replaced in the abdominal cavity, but he failed to recognise that it was the increased temperature of their new environment that caused these changes, and it was not until 1922 that Crew first suggested that the temperature factor was the operative one in the testicular atrophy of the cryptorchid. Since then a great deal of experimental work has confirmed these observations, and the fact now emerges that to ensure active spermatogenesia the testes must be kept at least 2° C. below the general body temperature, and, if this rule is not observed, spermatogenesis is at first temporarily depressed, and after a time completely and irreversibly destroyed. Hanley (1955) using a thermocouple needle has recorded a temperature difference of 4.5° C. between a testicle retained on the inguinal canal and its normally descended fellow.

These investigations not only demonstrate the deleterious effect of excessive temperature on spermatogenesis, but also emphasize the important part which the scrotum plays in the regulation of testicular temperature. The action of the cremaster and dartos muscles varies the position of the testes in relation to the body according to the temperature demands, and by this means any over-heating of the testes is prevented.

It is clear therefore that in cryptorchids permanent damage to spermatogenesis will occur if the condition is not relieved. Nelson (1950) has presented histological evidence that degeneration of germinal epithelium of the undescended testis does not occur until about the age of seven to eight years, and from this time on it is progressive until after puberty when total aplasia of the germinal epithelium results.

(2) *Acquired Injury to the Testes*

Traumatic injuries to the testes may be due to mechanical, thermal, X-ray, or radioactive agencies.

Direct mechanical injuries to the testes short of castration do not usually result in destruction of spermatogenesis; castration, however, obviously precludes any possibility of fertility, but it might be mentioned that, contrary

to popular belief, it does not necessarily destroy potency.

Thermal trauma has already been mentioned in connection with undescended testes. It has been shown, however, that impairment of spermatogenesis may occur as a result of raised testicular temperature brought about by such every-day means as scrotal supports and snug-fitting underpants which, by holding the testes in close contact with the body, create the unfavourable thermal environment.

There are two other local conditions which may be associated with lowered fertility, due most likely to their interference with the exacting temperature requirements of the testes, namely, varicocele and hydrocele. It has been shown by Davidson (1954) Russell (1955) and Tulloch (1955) that varicocele in particular is not infrequently associated with subfertility and that this is the result of the increased total scrotal temperature which varicocele occasions. This is further borne out by Hanley's observation that the temperature difference between a large varicocele and the rectal temperature in an otherwise normal male may be as little as 0.2° C.

Sustained hyperpyrexia for any length of time may also cause a temporary depression of spermatogenesis, but can hardly be cited as a cause of infertility.

The germinal epithelium of the testes is very sensitive to X-rays, and irradiation from radioactive substances, and either temporary or permanent spermatogenic arrest may result from exposure to them. The Sertoli and Leydig cells are, however, far more resistant and do not suffer material damage in doses crippling to the germinal elements.

(3) *Endocrine Disturbances*

Although there have been considerable advances in the knowledge and understanding of the individual glands and of their integrated function in the endocrine system as a whole, there still remain many unsolved problems, and the testis as an important member of the system is not exempt from these. It is hardly surprising therefore that the part played by endocrine disturbances in the production of infertility is also incompletely understood.

The endocrine axis primarily concerned with reproductive function comprises the pituitary and the testes. It is therefore not unreasonable to suppose that any depression of function affecting this axis may well produce one or another form of hypogonadism, and, according to the nature of the deficiency and the gland involved, so may various definite patterns of hypogandism be produced.

This supposition is to some extent correct as definite clinical syndromes associated with hypogonadism do exist. There are, however, many cases where this it not so, and particularly perplexing are those in which spermatogenic deficiencies occur, presumably of endocrine origin, but without any demonstrable stigmata of endocrine dysfunction. Between this group and the group which can be labelled as clinical syndromes are many intermediate degrees which are not easy to classify, and less easy to understand.

On the basis of gland dysfunction two main hypogonadal syndromes are described.

(1) Pituitary Hypogonadism.

(2) Primary Testicular Hypogonadism.

(1) *Pituitary Hypogonadism* may be of two types depending upon whether the hypofunction is total or limited to the gonadotrophin output by the anterior lobe.

Where there is total pituitary hypofunction, pan-hypopituitary hypogonadism results. If this is prepubertal in onset, dwarfism, sexual infantilism, myxoedema, and adrenal insufficiency result. Minor degrees of this condition are probably represented by those cases which are described under the heading of Fröhlich's syndrome. If on the other hand the onset is in adult life the syndrome commonly known as Simmond's disease occurs.

When the gonadotrophin output by the anterior lobe of the pituitary is below normal, hypogonadotrophic hypogonadism is the outcome, the clinical picture depending again upon the time of onset. Prepubertal onset results in a hypogonadal syndrome similar to that of the prepubertal eunuchoid which is usually characterised by the very tall, long-legged slender individual with markedly retarded secondary sexual characteristics.

Onset in adult life produces a very similar picture of that of the post-pubertal eunuchoid, where there is little retrogression of the secondary sexual characteristics, except that sterility ensues and potency is often absent; gynaecomastia and obesity are also common accompaniments.

(2) *Primary Testicular Hypogonadism,* as the term suggests, occurs when the testes themselves are primarily at fault. There is depression of interstitial cell activity and a deficiency in

androgen output. Eunuchoidism results, the type of which again depends on the stage of development of the individual at which it occurs. Three types of eunuchoidism are described: prepubertal, pubertal and post-pubertal. The general features of the pre- and post-pubertal varieties have already been mentioned. The pubertal form shows some evidence of secondary sexual characteristics, but their development is incomplete and is a halfway stage between the other two eunuchoid types.

There is a further type of testicular hypogonadism recently described, where the failure is reputed to be primarily tubular. This is known as hyaline tubular sclerosis, or the Klinefelter, Riefenstein, Albright-syndrome. It is a familial disease occurring about the age of puberty. Either gynaecomastia or eunuchoid features or both occur, and in all cases impotence and aspermatogenesis are present. The testes are small and biopsy reveals marked sclerosis of the tubules.

Apart from disturbances involving the pituitary-testicular axis other endocrine gland dysfunction may also affect fertility and in particular hypothyroidism and hyperadrenalism must be mentioned.

As already stated, to add to the complexity of the picture there are many gradations of the described syndromes, and also many atypical cases which are baffling even to the trained endocrinologist, and therefore usually incomprehensible to the average urologist.

Under the heading of endocrine disturbances mention must also be made of the male climateric, for which there is sufficient clinical and laboratory evidence to regard as a definite entity. It occurs in some men past middle age and is characterised by psychological and vasomotor disturbances, but infertility is affected only in so far as these men are usually impotent, a feature of this condition which must be distinguished from impotence due to psychoneurotic causes.

Finally there remains that large group of cases to which, unfortunately, the majority of patients seen in practice belong, namely those normal healthy men suffering from varying degrees of imperfect spermatogenesis, for which no cause can be found. It is possible that these cases are due to some subclinical endocrine disturbance, which in some may or other adversely affects the maturation of the germinal epithelium.

THE EVALUATION OF MALE INFERTILITY

Having briefly considered the physiology of reproductive function and the main etiological factors in its failure, it is necessary to consider the various methods at our disposal for evaluating this condition.

Needless to say, a complete history and thorough physical examination are just as essential in dealing with a case of infertility as with any other whose roots may lie in almost every system in the body. Owing to the rather special nature of this condition, however, there are certain aspects of the history and examination which must be emphasized as being of relatively greater importance than others. In addition there are certain further clinical and laboratory tests which are of great value, and, in some instances, indispensable to the evaluation of male infertility.

For reasons already mentioned it is of the utmost importance to obtain a full account of the patient's marital life, and when dealing with a husband who still retains the mid-Victorian attitude in all matters pertaining to sex, this may tax the doctor's tact and diplomacy to the utmost.

During the examination particular note should be made of any features which may suggest an underlying endocrine disturbance. The external genitalia likewise deserve particular scrutiny: the penis, for any evidence of hypogenitalism, congenital abnormality or other lesion, and the testes, for position, size, and in particular, consistency. Testes smaller than usual and of soft consistency are often associated with low or absent spermatogenesis. Hanley (1955) is in complete agreement with this view, and goes as far as to state that if a testis feels normal, a normal biopsy will invariably result, whereas if it feels atrophic a biopsy is hardly necessary to confirm the fact.

Associated varicocele or hydrocele are also of importance.

Any separation of the epididymis from the testis, cystic degeneration or other palpable abnormality must be sought for, and both spermatic cords carefully examined for vasal defects.

Special Investigations:

Over the years a number of special tests have been evolved for the study of male infertility, a few of which are essential for its accurate evaluation, and must always be employed; others however, although of value in special cases, are

mainly of academic and research interest and are not employed routinely.

The tests of special value are:—

(1) *The Post-Coital Examination of the Wife*

In spite of much that has been written to the contrary, this is one of the most useful preliminary investigations of the infertile couple. It is performed at the estimated time of ovulation and consists simply of the microscopic examination of the cervical mucous some 12 to 18 hours after intercourse. The presence of fifty or more highly motile sperms on two separate examinations is strongly suggestive that the male is not at fault. If on the other hand there are few or no motile sperms, the male partner should be more fully investigated. This test is simple and valuable as it not only affords evidence of potency and fertility, but does so without examination of the male, and its use therefore in cases where the husband refuses to submit to such examination is obvious.

(2) *Detailed Semen Analysis*

This is the most important single test in the study of male infertility and should be done in all cases.

Certain qualitative and quantitative features of the semen are considered important in evaluating fertility. These are as follows:

(*a*) *Volume* — the average volume is given as 3.5 cc., the normal range from 2 to 8 cc., and the suggested minimum 1.0 cc. Most of the fluid probably comes from the prostate. The significance of small volumes is difficult to assess, but when in very small amount may be due to occlusion of the ejaculatory ducts.

(*b*) *Viscosity* — normally, semen when first ejaculated is thick and viscid, but within half an hour liquifies. Increased viscosity is thought to impair sperm motility otherwise its effect on fertility is not known.

(*c*) *Motility* — 45 per cent. to 60 per cent. of the spermatozoa should be actively motile after two to six hours. The suggested minimum is 40 per cent.

(*d*) *Count* — the average normal count in millions per cc. of semen is about 140, the commonly accepted range of normality is 30 to 700 million per cc., and 20 million per cc. the suggested minimum. The extensive investigations of McLeod and Gold (1951) have shown that subfertility commences at the 20 million per cc. level, although conception cannot be precluded below that level as fertilization has occurred with counts of under 1 million per cc. Above the critical 20 million per cc. level the chances of conception do not rise proportionately with increase of sperm count. It appears also that it is the density per cc. that matters and not the total sperm count.

(*e*) *Morphology* — this is studied either in the fresh or stained specimen. The average number of abnormal forms is about 10 per cent., the normal range being from 6 to 25 per cent. More than 25 per cent. of abnormal forms is considered corroborative evidence of sub-fertility.

In evaluating the results obtained from a semen analysis, no single value, unless grossly abnormal, appears to be more important than any other; all aspects are important. Finally, the results of two separate semen specimens must be to hand before any prognostications are made.

(3) *Testicular Biopsy*

In spite of Hanley's contention that testicular biopsy is usually unnecessary, the general consensus of opinion is that it has a very real value in the evaluation of testicular defects and provides an excellent yardstick for the institution of corrective measures or in the witholding of treatment in cases where the biopsy reveals a hopeless prognosis for fertility. Biopsy is indicated in patients with azoospermia and persistent oligozoospermia, as by this means only can it be definitely ascertained whether spermatogenesis is present or not. This is of great value in determining whether or not paucity or absence of sperm in the semen is due to obstructive lesions of the spermatic tract or testicular defect. The accurate interpretation of testicular biopsies is difficult and requires a special knowledge and understanding of testicular pathology.

Amongst the tests which are not routinely employed but which are of use in special cases only, the following may be mentioned.

Urinary gonadotrophin assay. Here the urinary content of follicle stimulating hormone is obtained by biological tests, and by this means hypopituitary and primary testicular hypogonadism may be differentiated. 17-Ketosteroid excretion in the urine and seminal vesiculography are also reserved for special cases.

TREATMENT:

The various methods of treating subfertility and sterility in the male have been:

(1) *General Measures*

It is well known that the stress and strain of modern life may impair fertility not only by the psychological upheavals which it engenders,

but also by the general lowering of health and vitality which it may produce. In cases of impotence of psychoneurotic origin simple psychotherapeutic measures may be successful, if not the aid of a competent psychotherapist may be necessary. The building up of general health and resistance is also of value.

There is ample experimental evidence that gross deficiencies of vitamins E, A and B may result in material damage to the reproductive tract of both male and female. In everyday practice, however, such deficiencies are rarely encountered, and therefore vitamin therapy must play little part in the management of fertility.

(2) *Endocrine Therapy*

It is reasonable to suppose that appropriate endocrine therapy should be effective in cases where deficiency can be demonstrated, be it of the pituitary, testis, or thyroid.

Thus in the treatment of panpituitary hypogonadism it is rational to give pituitary gonadotrophins, thyroid and adrenal cortical extract; likewise the treatment of hypogonadotrophic hypogonadism should be with pituitary gonadotrophins alone, and in primary testicular hypogonadism testosterone should have the desired effect. Finally hypothyroidism causing spermatogenic depression is treated with thyroid extract. In all these conditions there may be improvement in the general clinical picture as a result of this hormone therapy, but, in so far as the associated spermatogenic deficiencies are concerned, the results of therapy, with the notable exception of hypothyroidism, have been most disappointing.

There are, however, two conditions where some response to endocrine therapy may be obtained. The one is the normal healthy subfertile oligozoospermic male with a germinal epithelium which on biopsy does not show gross defect. In these cases testosterone therapy is indicated, the usual dosage being 100 mg. of long-acting depot-testosterone by intramuscular injection weekly, for six to eight weeks. This is followed by a definite depression in the sperm count which, for some unknown reason, is followed some six months later by a marked increase in spermatogenic activity, known as the rebound phenomenon, producing sperm counts often far in excess of the earlier levels. Although this method is not effective in every instance, the fact that a proportion of cases do show a sustained satisfactory response makes it worthy of trial, more particularly as there is nothing to be lost, and possibly a lot to be gained.

During the rebound phase it would seem to me rational to give a course of pituitary gonadotrophins in the hopes that both intestitial and germinal cell activity may thereby be further boosted. An empirical dosage of 100 mg. by injection twice weekly for 15 weeks may be given, and at the conclusion of the treatment a further semen analysis should be made to assess the results of treatment.

The other condition which responds to testosterone therapy is the male climateric. The symptoms are relieved and potency restored and the results are usually so good that it serves as a therapeutic test to distinguish the impotence of the male climateric from that of psychogenic origin which is unaffected by testosterone.

(3) *Surgical Measures*

The surgery of male infertility is a subject unto itself, but time and the imposition I have made on your attention forbids more than a bare summary of the surgical treatment of this condition.

There are, as already mentioned, a number of conditions which by causing impotence result in infertility, and some of these are amenable to surgical treatment. The correction of congenital anomalies of the penis, and the treatment of urethral stricture are instances of these.

Some of the obstruction lesions of the seminal ducts may be successfully treated by surgical intervention. Examples of these are the reconstitution of the vas after either accidental or deliberate division. Section of the vas does not destroy spermatogenesis in the testis, and Hanley (1955) quotes four personal successful cases of surgical reconstitution of the vas after deliberate section several years before — all had sperms in the ejaculate two months after operation.

Congenital and inflammatory occlusion of the vas, if limited in extent, may be excised and the vas reconstituted

Similar lesions occur in the epididymal duct, and the post-inflammatory ones in particular often occur in the region of the body or tail. These cases lend themselves to epididymovasostomy whereby the patent vas is anastomosed to the head of the epididymis, thus by-passing the obstructed area. A prerequisite to the success of this procedure is the demonstration of live sperms in the head of the epididymis, but even in spite of this the results of this procedure are not good.

Those conditions which result in an altered thermal environment for the testes are in most cases amenable to surgical correction.

Tulloch (1955) has produced some remarkable results following the surgical treatment of varicocele in patients with associated subfertility. Of the 30 cases reported, 10 returned to normal fertility with subsequent successful pregnancy, and of these, two patients were initially azoospermic. In a further 10 cases there was considerable improvement in the sperm count mostly to above the "infertile" level, but at the time of writing no pregnancy had occurred. The remaining 10 cases were considered failures. From these results it is justifiable that, where subfertility and varicocele coexist, the varicocele should be treated.

The correction of bilateral undescended testes before puberty may prevent otherwise certain sterility. Bilateral orchiopexy, however, even when performed at the optimum age of six to seven years is not often followed by normal spermatogenesis, the result being purely cosmetic.

(4) *Artificial Insemination*

The use of semen of the subfertile for artificial insemination may be attended with success. Its value lies in that the greater part of the ejaculate can with certainty be made to come into contact with the cervical os. Patients on the borderline of fertility with counts of about 20 million per cc. are good candidates for this.

PROGNOSIS

In general the prognosis with regard to male infertility is poor. This is largely due to the fact that only in a small percentage of cases can the cause be determined, and, until this difficulty can be overcome it seems that the outlook must remain bleak.

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